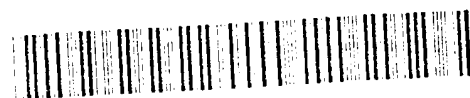


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0 355 460 A3

Publication number:

EUROPEAN PATENT APPLICATION

Application number: 89113852.1

Int. Cl.⁵ C12N 15/18, C12P 21.02,
C07K 3 08, A61K 37 36

Date of filing: 27.07.89

Priority: 24.08.88 US 236060
03.07.89 US 372699

Date of publication of application:
28.02.90 Bulletin 90/09

Designated Contracting States:
AT BE CH DE ES FR GB GR IT LI LU NL SE

Date of deferred publication of the search report:
03.04.91 Bulletin 91/14

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Stabilization of somatotropins by modification of cysteine residues utilizing site directed mutagenesis or chemical derivatization.

The present invention relates to novel modified or derivatized recombinant animal somatotropins. This invention also provides methods for stabilizing recombinant animal somatotropins by modification or deletion of the Cysteine residues utilizing site directed mutagenesis to replace from one to four of the cysteine amino acid residues of said somatotropins with one or more different amino acid residues or by derivatization of (1) both cysteine amino acid residues in the small loop of said somatotropin, both cysteine amino acid residues in the large loop or the four cysteine amino acid residues in both loops of said somatotropin.

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EUROPEAN SEARCH REPORT

Application Number

EP 89 11 3852

| DOCUMENTS CONSIDERED TO BE RELEVANT | | | |
|---|--|--|---|
| Category | Citation of document with indication, where appropriate, of relevant passages | Relevant to claim | CLASSIFICATION OF THE APPLICATION (Int. Cl.5) |
| Y | EP-A-0 192 811 (CETUS CORP.) * Entire document * | 1-35 | C 07 K 13 00 C 12 N 15 18 C 07 K 3 08 |
| X | --- | 1,2,28,34,35 | A 61 K 37 36 C 12 P 21 02 |
| Y | EUR. J. BIOCHEM., vol. 153, 1985, pages 445-449; T. TOKUNAGA et al.: "Synthesis and expression of a human growth hormone (somatotropin) gene mutated to change cysteine-165 to alanine" * Entire article * | 1-35 | |
| Y | --- | | |
| Y | BIOCHEMISTRY, vol. 25, 1986, pages 6907-6917, American Chemical Society; T.F. HOLZMAN et al.: "Reoxidation of reduced bovine growth hormone from a stable secondary structure" * Entire article * | 1-35 | |
| Y | --- | | |
| Y | BIOLOGICAL ABSTRACTS, vol. 85, no. 9, 1988, abstract no. 88990, Philadelphia, PA, US; J.J. CARIDAD et al.: "Selective reduction of the disulfide bonds of ovine placental lactogen", & INT. J. PEPT. PROTEIN RES. 31(1): 71-76, 1988 | 1-35 | |
| E | WO-A-9 002 758 (PITMAN-MOORE INC.) * Entire document * | 1,4-27, 31,34-35 | |
| | ----- | | |
| The present search report has been drawn up for all claims | | | TECHNICAL FIELDS SEARCHED (Int. Cl.5) |
| | | | C 07 K C 12 N C 12 P A 61 K |
| Place of search | | Date of completion of search | Examiner |
| The Hague | | 22 January 91 | GROENENDIJK M S M. |
| CATEGORY OF CITED DOCUMENTS | | | |
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